Status of the claims

Claims 1 and 20 have been amended to delete the term "sensory" and to recite the term "taste." This amendment adds no new matter. Support for this amendment can be found, e.g., in the specification on page 4, lines 1-11.

Rejection under 35 U.S.C. § 112, second paragraph

"Physical effect" or "chemical effect"

Claim 3 was rejected as allegedly indefinite for reciting the phrase "functional effect is a chemical effect." Claim 4 was rejected as allegedly indefinite for reciting the phrase "functional effect is a physical effect." Applicants respectfully traverse. The specification describes that functional effects can be measured in a variety of ways known to those of skill in the art (*see, e.g.*, specification, page 13, lines 3-14 and page 25, lines 25-31). Functional effects are defined by the specification as parameters that are directly or indirectly under the influence of the claimed G-protein beta subunit. As described in the specification, functional effects include physical effects, such as binding, changes in shape, etc., as well as chemical effects, such as changes in intracellular calcium levels, etc. The phrases "chemical effect" and "physical effect" therefore meet the threshold requirements of clarity and precision, as required by the statute (see, e.g., MPEP § 2173.02). Applicants therefore respectfully request that the rejection be withdrawn.

"Promiscuous G-protein"

Claim 20 was rejected as allegedly indefinite for reciting the phrase "promiscuous G-protein." Applicants respectfully traverse. The use of the term "promiscuous" with respect to a G-protein subunit is well known to those of skill in the art (*see, e.g.*, Offermanns & Simon, *J. Biol. Chem.* 270:15175-15180 (1995). Furthermore, the specification defines such promiscuous G-proteins as those that are expressed in heterologous cells and "allow coupling of a wide range of receptors" (*see, e.g.*, specification, page 32, lines 22-32). The phrase "promiscuous G-protein" therefore meets the threshold requirements of clarity and precision, as required by the statute (see, e.g., MPEP § 2173.02). Applicants therefore respectfully request that the rejection be withdrawn.

Rejection under 35 U.S.C. § 103

Claims 1-20 were rejected as allegedly obvious over Margolskee in view of Ray or Levine. Margolskee discloses Gustducin, a G-protein alpha subunit specifically expressed in taste cells. Margolskee also teaches generally that compounds that modulate taste may be identified using assays for taste cell specific proteins involved in taste transduction, such as Gustducin. Margolskee does not disclose the taste cell specific G-protein beta subunits of the present invention. Ray and Levine disclose G-protein beta subunits with identity to the claimed polypeptides. The polypeptide of Ray was cloned from a heart cDNA library, and expression of the mRNA encoding the G-protein beta subunit was shown in heart and brain. The polypeptide of Levine was cloned from a retina cDNA library, and expression was shown in four different cell lines: rhabdomyosarcoma, pheochromocytoma, neuroblastoma, and dermal fibroblasts. Neither Ray nor Levine disclose that the G-protein beta subunit is expressed in taste cells of the tongue.

To expedite prosecution, Applicants have amended the claims to clarify that the claimed polypeptides are specifically expressed in "taste" cells. To the extent that the rejection applies to the claims as amended, Applicants respectfully traverse. The present invention demonstrates for the first time a G-protein beta subunit preferentially expressed in taste cells of the tongue. As such polypeptides were not previously known to be expressed in the tongue and involved in taste signal transduction, one of skill in the art would not have been motivated to use the proteins of Ray and Levine in the taste transduction assay methods of Margolskee.

In the rejection, the Examiner concludes that the presently claimed invention would be obvious, without identifying the principles that would motivate one of skill in the art to combine the cited references. By using hindsight to provide the requisite motivation, the Examiner has failed to make a prima facie case of obviousness. *In re Rouffet*, 47 USPQ2d 1453 (Fed. Cir. 1998). As discussed by the Federal Circuit in *In re Rouffet*,

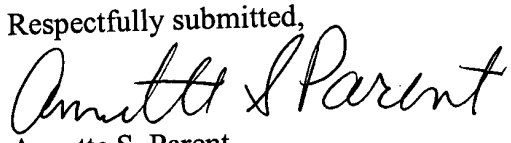
> Because the Board did not explain the specific understanding or principle within the knowledge of a skilled artisan that would motivate one with no knowledge of Rouffet's invention to make the combination, this court infers that the examiner selected these references with the assistance of hindsight. This court forbids the use of hindsight in the selection of references that comprise the case of obviousness" (*In re Rouffet,* 47 USPQ2d at 1458).

Ray teaches a G-protein beta subunit that has 100% identity to SEQ ID NO:3 of the present invention. Levine teaches a G-protein beta subunit that has 97% identity to SEQ ID NO:5 of the present invention. However, the protein of Ray was cloned from a heart cDNA library, while the protein of Levine was cloned from a retina cDNA library. Expression of these polypeptides were shown in the heart and brain (Ray) and in in four different cell lines: rhabdomyosarcoma, pheochromocytoma, neuroblastoma, and dermal fibroblasts (Levine). Notably, these references fail to teach or suggest that these G-protein beta subunits are expressed in taste cells, or are in any way involved in taste signal transduction. Therefore, one of skill in the art would not be motivated to use the polypeptides of Ray and Levine in the taste transduction assays of Margolskee. Margolskee only provides general guidance regarding taste transduction assays, and fails to teach the polypeptides of the invention. The cited references, either alone or in combination, thus fail to teach or disclose the claimed invention. Applicants therefore respectfully request that the rejection be withdrawn.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance and an action to that end is urged. If the Examiner believes a telephone conference would aid in the prosecution of this case in any way, please call the undersigned at 415-576-0200.

Respectfully submitted,



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APPENDIX A

VERSION WITH MARKINGS TO SHOW CHANGES MADE

1. (once amended) A method for identifying a compound that modulates [sensory] taste signaling in [sensory] taste cells, the method comprising the steps of:

(i) contacting the compound with a [sensory] taste cell specific G-protein beta polypeptide, the polypeptide comprising greater than 70% amino acid sequence identity to an amino acid sequence of SEQ ID NO:3 or SEQ ID NO:5; and

(ii) determining the functional effect of the compound upon the polypeptide.

20. (once amended) A method for identifying a compound that modulates [sensory] taste signaling in [sensory] taste cells, the method comprising the steps of:

(i) expressing a [sensory] taste cell specific G-protein beta polypeptide in a host cell, wherein the G-protein beta polypeptide has greater than 70% amino acid sequence identity to a polypeptide having a sequence of SEQ ID NO:3 or SEQ ID NO:5;

(ii) expressing a promiscuous G-protein alpha polypeptide and a [sensory] taste cell specific G-protein coupled receptor in the host cell,

(iii) contacting the host cell with the compound that modulates [sensory] taste signaling in [sensory cells] taste; and

(iv) determining changes in intracellular calcium levels in the host cell, thereby identifying the compound that modulates [sensory] taste signaling in [sensory] taste cells.

APPENDIX B

PENDING CLAIMS

1. (once amended) A method for identifying a compound that modulates taste signaling in taste cells, the method comprising the steps of:

(i) contacting the compound with a taste cell specific G-protein beta polypeptide, the polypeptide comprising greater than 70% amino acid sequence identity to an amino acid sequence of SEQ ID NO:3 or SEQ ID NO:5; and

(ii) determining the functional effect of the compound upon the polypeptide.

2. (as filed) The method of claim 1, wherein the polypeptide specifically binds to polyclonal antibodies generated against SEQ ID NO:3 or SEQ ID NO:5.

3. (as filed) The method of claim 1, wherein the functional effect is a chemical effect.

4. (as filed) The method of claim 1, wherein the functional effect is a physical effect.

5. (as filed) The method of claim 1, wherein the functional effect is determined by measuring changes in intracellular cAMP, cGMP, IP3, DAG, or Ca2+.

6. (as filed) The method of claim 5, wherein the changes in intracellular cAMP or cGMP are measured using immunoassays.

7. (as filed) The method of claim 1, wherein the functional effect is determined by measuring binding of radiolabeled GTP to a G protein comprising the polypeptide, or to the polypeptide.

8. (as filed) The method of claim 1, wherein the functional effect is determined by measuring changes in intracellular Ca2+.

9. (as filed) The method of claim 1, wherein the polypeptide is expressed in a cell or cell membrane.

10. (as filed) The method of claim 9, wherein the functional effect is determined by measuring changes in the electrical activity of the cell or the cell membrane expressing the polypeptides.

11. (as filed) The method of claim 10, wherein the changes in the electrical activity are measured by an assay selected from the group consisting of a voltage clamp assay, a patch clamp assay, a radiolabeled ion flux assay, and a fluorescence assay using voltage sensitive dyes.

12. (as filed) The method of claim 9, wherein the cell is a eukaryotic cell.

13. (as filed) The method of claim 1, wherein functional effect is determined by measuring changes in the level of phosphorylation of taste cell specific proteins.

14. (as filed) The method of claim 1, wherein the functional effect is determined by measuring changes in transcription levels of taste cell specific genes.

15. (as filed) The method of claim 1, wherein the polypeptide is linked to a solid phase.

16. (as filed) The method of claim 15, wherein the polypeptide is covalently linked to a solid phase.

17. (as filed) The method of claim 1, wherein the polypeptide is recombinant.

18. (as filed) The method of claim 1, wherein the polypeptide is from a human, a mouse or a rat.

19. (as filed) The method of claim 1, wherein the polypeptide has an amino acid sequence of SEQ ID NO:3 or SEQ ID NO:5.

20. (once amended) A method for identifying a compound that modulates taste signaling in taste cells, the method comprising the steps of:

(i) expressing a taste cell specific G-protein beta polypeptide in a host cell, wherein the G-protein beta polypeptide has greater than 70% amino acid sequence identity to a polypeptide having a sequence of SEQ ID NO:3 or SEQ ID NO:5;

(ii) expressing a promiscuous G-protein alpha polypeptide and a taste cell specific G-protein coupled receptor in the host cell,

(iii) contacting the host cell with the compound that modulates taste signaling in taste; and

(iv) determining changes in intracellular calcium levels in the host cell, thereby identifying the compound that modulates taste signaling in taste cells.